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EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/613,006	SCHENA, MARK A.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2, 3* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-24 are indefinite in Claim 1 for the recitation "each location on the surface corresponds essentially to a single genomic segment" because both terms "corresponds" and "essentially" are both non-specific relational terms and therefore the relationship between "each location" and "genomic segment" is undefined. It is suggested that Claim 1 be amended to define the relationship e.g. replace "corresponds essentially" with "hybridizes" or "is complementary".

b. Claims 1-24 are indefinite in Claim 1 in lines 7-8 because "material on the surface" lacks proper antecedent basis in the amplified genomic segments in the preceding step and therefore the relationship between the "material" and "genomic segments" is undefined. It is suggested that Claim 1 be amended to provide proper antecedent basis e.g. define the relationship between the "material" and "genomic segments".

c. Claims 1-24 are indefinite in Claim 1 for the recitation "hybridizing the microarray with a mixture of synthetic oligonucleotides.....to the genomic segments" because it is unclear how the "mixture" relates to the "amplified genomic segments" and how the "mixture relates to the "material" on the "microarray". It is suggested that Claim 1 be amended to define the relationships e.g. in line 6 after "polymerase chain reaction primers" insert "to form a mixture of synthetic oligonucleotides".

d. Claims 1-24 are indefinite in Claim 1 for the recitation "deriving genotyping information..." because the claims are drawn to a method of genotyping but the claim does not recite a step of genotyping. It is suggested that Claim 1 be amended to clarify e.g. at the end the final step insert "to thereby genotype the multiple samples".

e. Claims 1-24 are indefinite in Claim 1 for the recitation "detecting signals from the hybridized microarray" because "signals" lacks proper antecedent basis in the claim because the preceding steps of the claim do not recite a signal-producing element e.g. label. It is suggest that Claim 1 be amended to provide proper antecedent basis.

f. Claim 2 is indefinite in the recitation "polymerase chain reaction primers such that the genomic segments comprise distinct genetic loci" because "such that" is a non-specific relational phrase and therefore it is unclear how the primers relate to the loci. It is suggested that the claim be amended to clarify e.g. replace "such that the" with "to thereby amplify".

g. Claim 8 is indefinite in the recitation "wherein the density" because the recitation lack proper antecedent basis in Claim 1. It is suggested that the claim be amended to provide proper antecedent basis e.g. replace "the density of the microarray on the surface is" with the surface of said microarray comprises".

h. Claim 8 is indefinite in the recitation "1000 spots per square centimeter" because "spots" lacks proper antecedent basis in Claim 1. It is suggested that the claim be amended to provide proper antecedent basis e.g. replace "spots" with "locations".

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 8-9, 12-13, 15-16 and 21 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wang et al. (Science, 1998, 280: 1077-1082). As stated above, Claim 1 is indefinite because it is unclear how the amplified genomic segments relate to the material on the array and the synthetic oligonucleotides and it is unclear what material is on the array i.e. the amplified genomic segments or the synthetic oligonucleotides. For purposes of examination, the claim is interpreted to recite that the genomic segments are amplified to thereby produce the synthetic oligonucleotides which are hybridized to the material on the array.

Regarding Claim 1, Wang et al. disclose a method of simultaneously genotyping multiple samples, the method comprising: amplifying genomic segments from a plurality of samples using polymerase chain reaction primers, each genomic segment comprising a genetic locus; forming a microarray on a surface wherein material at each location on the surface corresponds to a single genomic segment from a single sample; hybridizing the microarray with a mixture of synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segments; and deriving genotyping information for multiple sample simultaneously by detecting signals from the hybridized microarray (page 1078, right column, first full paragraph).

Regarding Claim 2. Wang et al. disclose the method wherein the polymerase chain reaction primers comprise a plurality of distinct polymerase chain reaction primers such that the genomic segments comprise distinct genetic loci (page 1081, right column, 16.) and genotyping information is derived simultaneously for multiple genetic loci from multiple samples (page 1078, right column first and second paragraphs).

Regarding Claim 3, Wang et al. disclose the method wherein the plurality of samples comprises at least 10 distinct samples (page 1080, right column, first full paragraph).

Regarding Claim 8, Wang et al. disclose the method wherein the microarray comprises at least 1000 spots per square centimeter (page 1078, left column last paragraph and page 1081, right column 14).

Regarding Claim 9, Wang et al. disclose the method wherein the mixture of synthetic oligonucleotides comprises ten different oligonucleotide sequences (page 1080, right column).

Regarding Claim 12, Wang et al. disclose the method wherein hybridizing is performed in an aqueous solution comprising salts and detergent (page 1081, right column 16., last 7 lines).

Regarding Claim 13, Wang et al. disclose the method wherein hybridizing is performed at a temperature about 10 °C below the melting temperature of the synthetic oligonucleotides (page 1081, right column 16., last 7 lines and page 1082, left column, 25., lines 1-4).

Regarding Claim 15, Wang et al. disclose the method wherein the synthetic oligonucleotides comprise non-fluorescent labels i.e. biotin (page 1081, right column 16.).

Regarding Claim 16, Wang et al. disclose the method wherein the genotyping information distinguishes sample from homozygotes and samples from heterozygotes at a specific genetic locus (page 1078, Table 1 and page 1082, 28.).

Regarding Claim 21, Wang et al. disclose the method wherein surface comprises glass (page 1078, left column last paragraph).

5. Claims 1, 2, 8, 12, 21 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by Lashkari et al. (Proc. Natl. Acad. Sci. USA, 1997, 94: 13057-13062). As stated above, Claim 1 is indefinite because it is unclear how the amplified genomic segments relate to the material on the array and the synthetic oligonucleotides and it is unclear what material is on the array i.e. the amplified genomic segments or the synthetic oligonucleotides. For purposes of

examination, the claim is interpreted to recite that the amplified genomic segments are the material on the array and the synthetic oligonucleotides are hybridized to the amplified genomic segments.

Regarding Claim 1, Lashkari et al. disclose a method of simultaneously genotyping multiple samples, the method comprising: amplifying genomic segments from a plurality of samples using polymerase chain reaction primers, each genomic segment comprising a genetic locus; forming a microarray on a surface wherein material at each location on the surface corresponds to a single genomic segment from a single sample; hybridizing the microarray with a mixture of synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segments; and deriving genotyping information for multiple sample simultaneously by detecting signals from the hybridized microarray (page 13057, left column, last paragraph-right column first paragraph).

Regarding Claim 2. Lashkari et al. disclose the method wherein the polymerase chain reaction primers comprise a plurality of distinct polymerase chain reaction primers such that the genomic segments comprise distinct genetic loci (page 13057, right column, second full paragraph) and genotyping information is derived simultaneously for multiple genetic loci from multiple samples (page 13059, left column, last paragraph).

Regarding Claim 8, Lashkari et al. disclose the method wherein the microarray comprises at least 1000 spots per square centimeter (page 13058, right column, first full paragraph).

Regarding Claim 12, Lashkari et al. disclose the method wherein hybridizing is performed in an aqueous solution comprising salts and detergent (page 13058, left column third full paragraph).

Regarding Claim 21, Lashkari et al. disclose the method wherein surface comprises glass (page 13058, right column, second full paragraph).

Regarding Claim 24, Lashkari et al. disclose the method wherein the microarray is formed by mechanical micro-spotting (page 13057, right column, last paragraph).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-4, 12-18, 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, 1998, 280: 1077-1082) in view of Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998).

Regarding Claims 1-4, Wang et al. teach the method of simultaneously genotyping multiple samples, the method comprising: amplifying genomic segments from a plurality of samples using polymerase chain reaction primers, each genomic segment comprising a genetic locus; forming a microarray on a surface wherein material at each location on the surface corresponds to a single genomic segment from a single sample; hybridizing the microarray with a mixture of synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segments; and deriving genotyping information for multiple sample simultaneously by detecting signals from the hybridized microarray wherein the samples comprises at least 10 distinct samples (page 1080, right column, first full paragraph) wherein the polymerase chain reaction primers comprise a plurality of distinct polymerase chain reaction primers such that the genomic segments comprise distinct genetic loci (page 1081, right column, 16.) and genotyping information is derived simultaneously for multiple genetic loci from multiple samples (page 1078, right column first and second paragraphs) and

wherein the plurality of samples comprises at least 10 distinct samples (page 1080, right column, first full paragraph) but they do not teach the plurality of samples comprises at least 5,000 distinct samples. Brown et al. teach a similar method comprising amplifying genomic segments from a plurality of samples; forming a microarray on a surface wherein material at each location on the surface corresponds to a single genomic segment; hybridizing the microarray with a mixture of synthetic oligonucleotides complementary to the genomic segments; and deriving genotyping information for the multiple samples simultaneously by detecting signals from the hybridized array, wherein the plurality of samples comprise at least 96 distinct samples and they teach processing multiple samples simultaneously provides significant saving of time and money (Column 15, lines 19-43). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to the multiple samples of Wang et al. by increasing the number of samples to at least 5,000 for the expected benefit of processing multiple samples as taught by Brown et al. i.e. significant saving of time and money (Column 15, lines 39-43).

Regarding Claim 8, Wang et al. disclose the method wherein the microarray comprises at least 1000 spots per square centimeter (page 1078, left column last paragraph and page 1081, right column 14).

Regarding Claim 9, Wang et al. disclose the method wherein the mixture of synthetic oligonucleotides comprises ten different oligonucleotide sequences (page 1080, right column).

Regarding Claim 12, Wang et al. disclose the method wherein hybridizing is performed in an aqueous solution comprising salts and detergent (page 1081, right column 16., last 7 lines).

Regarding Claim 13, Wang et al. disclose the method wherein hybridizing is performed at a temperature about 10 °C below the melting temperature of the synthetic oligonucleotides (page 1081, right column 16., last 7 lines and page 1082, left column, 25., lines 1-4).

Regarding Claim 14, Wang et al. disclose the method wherein the synthetic oligonucleotides comprise non-fluorescent labels i.e. biotin (page 1081, right column 16.) but they do not teach fluorescent labels. However, Brown et al. teach the similar method wherein the synthetic oligonucleotides comprise fluorescent labels (Column 15, lines 35-39).

Regarding Claim 15, Wang et al. disclose the method wherein the synthetic oligonucleotides comprise non-fluorescent labels i.e. biotin (page 1081, right column 16.).

Regarding Claim 16, Wang et al. disclose the method wherein the genotyping information distinguishes sample from homozygotes and samples from heterozygotes at a specific genetic locus (page 1078, Table 1 and page 1082, 28.).

Regarding Claim 17, Brown et al. teach the method wherein the signal are generated by fluorescence emission from the labeled oligonucleotides (Column 16, lines 66-67).

Regarding Claim 18, Brown et al. teach the method wherein the signals are generated by fluorescence emission at more than one wavelength of light (Column 17, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the non-fluorescent labels of Wang et al. with the fluorescent labels of Brown et al. based on availability of fluorescence-detection equipment and to label the oligonucleotides with fluorescent labels to thereby use the available fluorescence-detection equipment for the expectant benefit of economy as taught by Brown et al. (Column 15, lines 48-51). The skilled practitioner in the art would have been further motivated to detect the fluorescence emission from the labeled oligonucleotides using the available equipment to detect labeled oligonucleotides hybridized on the array. One skilled in the art would have been further motivated to label oligonucleotides with labels that fluoresce at more than one wavelength to thereby differentially label the oligonucleotides e.g. oligonucleotides from each sample are labeled with a different fluorescent label, for the obvious benefit of differentially detecting oligonucleotides from each sample.

Regarding Claim 21, Wang et al. disclose the method wherein surface comprises glass (page 1078, left column last paragraph).

Regarding Claim 24, Wang et al. do not teach the method wherein the microarray is formed by mechanical microspotting. However, Brown et al. teach the similar method wherein the microarray is formed by mechanical microspotting (Column 7, lines 1-34). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microarray formation of Wang et al. with the mechanical microspotting of Brown et al. for the expected benefit of automated, rapid and exact formation of the microarray as taught by Brown et al. (Column 53-67).

8. Claims 5-7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, 1998, 280: 1077-1082) in view of Cheng et al. (Clin. Chem. Lab. Med, 1998, 36(8): 561-566).

Regarding Claim 5, Wang et al. teach the method wherein the genomic segments comprise single-nucleotide polymorphism (Abstract) but they do not teach the genomic segments comprise human disease loci. However, it was known in the art at the time the claimed invention was made that a single-nucleotide polymorphism may represent a disease loci as taught by Cheng et al. who teach a similar for simultaneously genotyping multiple samples comprising: amplifying genomic segments; forming a microarray; hybridizing the microarray with a mixture of synthetic oligonucleotides; and deriving genotyping information for the multiple samples (page 562, right column last paragraph) wherein the genomic segments comprise human disease loci (page 562, Table 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the disease loci teaching of Cheng et al. to the genomic segments in the method of Wang et al. for the expected benefit of disease-specific genotyping of human samples to thereby provide large-scale

screening for human disease as taught by Wang et al. (page 1081, middle column, last paragraph).

Regarding Claim 6, Wang et al. do not teach the samples are a neonatal and Cheng et al. do not teach the samples are neonatal. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the disease-specific genotyping of human samples of Wang et al. and Cheng et al. to genotype neonatal human samples for the obvious benefit of diagnosing disease early in life (i.e. neonatal) to thereby provide disease-specific clinical treatments and or preventive measures.

Regarding Claim 7, Wang et al. and Cheng et al. do not teach the genetic loci are selected from the group consisting of β-globin, CFTR and GALT. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the disease-specific genotyping of human samples of Wang et al. and Cheng et al. to genotype using disease-specific loci known to be associated with disease i.e. β-globin, CFTR and GALT for the expected benefit of disease-specific genotyping of human samples to thereby provide large-scale screening for human disease as taught by Wang et al. (page 1081, middle column, last paragraph).

Regarding Claim 11, Wang et al. do not teach the length of the genomic segments. However, Cheng et al. teach the similar method wherein the genomic segments comprise between about 40 and 1000 base pairs (page 562, right column, second paragraph, lines 14-15).

9. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, 1998, 280: 1077-1082).

Regarding Claim 10, Wang et al. teach the synthetic oligonucleotides are short (page 1082, left column 21.) but they do not teach the oligonucleotides are between about 10 and 30 nucleotides. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the short genomic segment teaching of Wang et al. and using routine experimentation derive and use genomic segments of 10 to 30 nucleotides in length for the obvious benefit of optimizing experimental conditions to thereby maximize experimental results.

10. Claims 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, 1998, 280: 1077-1082) in view of Brown et al. (U.S. Patent No. 5,807,522, issued 15 September 1998) and Fodor et al. (U.S. Patent No. 5,800,992, filed 25 June 1996).

Regarding Claims 19-20, Wang et al. teach the signals are generated by fluorescence at more than one wavelength (page 1082, left column, lines 1-10) and Brown et al. teach the similar method wherein the signals are generated by fluorescence emission at more than one wavelength (Column 17, lines 1-8) but Wang et al. and Brown et al. do not teach the emission after antibody staining. However, signals generated by fluorescence emission after antibody staining (Claim 19) and at more than one wavelength (Claim 20) was well known and routinely practiced in the art at the time the claimed invention was made as taught by Fodor et al. (Column 51, lines 50-57 and Column 52, lines 3-9). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the more than one fluorescence emission techniques of Wang et al. and Brown et al. with the fluorescent emission after antibody staining as routinely practiced in the art based on available reagents

and for the known benefits of antibody labeling i.e. commercially available and simple and therefore for the expected benefits of ease and economy.

11. Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (Science, 1998, 280: 1077-1082) in view of Pease et al. (Proc Natl. Acad. Sci. USA, 1994, 91: 5022-5026).

Regarding Claims 22-23, Wang et al. teach their microarray formed according to the teaching of Pease et al. (page 1078, left column, last paragraph). Pease et al. teach the microarray wherein the genomic segments comprise amino linkers (page 5024, left column third full paragraph) and the surface comprises reactive aldehyde groups (page 5023, right column, last paragraph).

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
May 17, 2001

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